Lactate Production and Measurement in Critically Ill Horses

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Abstract: Blood lactate concentration can be easily measured by practitioners using inexpensive point-of-care meters. Anaerobic tissue metabolism resulting from inadequate oxygen delivery (DO2) is the most important cause of an increase in blood lactate concentration in equine patients. However, hyperlactatemia also occurs under conditions of apparently adequate DO2, usually in association with sepsis and an intense inflammatory reaction. Numerous mechanisms have been proposed for aerobic hyperlactatemia, including increased Na+/K+-ATPase activity in response to inflammatory mediators; inhibition of pyruvate dehydrogenase, a key enzyme in glucose metabolism; and increased lactate production by activated inflammatory cells. The liver is responsible for most lactate metabolism, and liver disease might contribute to an increase in blood lactate concentration in some patients. Skeletal muscle is usually considered the most important source of lactate during sepsis. The roles of the lungs and the gastrointestinal tract in lactate production have been investigated but remain uncertain.

Lactate Production

Lactate Production in Health
Under normal conditions, production of adenosine 5’-triphosphate (ATP), the cell’s primary energy source, from glucose occurs in two sequential pathways: glycolysis and the citric acid cycle (also known as the Krebs cycle or tricarboxylic acid cycle)1,2 (FIGURE 1). Although a small amount of ATP is produced by glycolysis, the vast majority is generated by oxidative phosphorylation of intermediates produced during the citric acid cycle. Glycolysis converts a single molecule of glucose into two molecules of pyruvate in a 10-step process within cytoplasm.1,2 This sequence of reactions does not require oxygen and generates two molecules of ATP and hydrogen ions. Glycolysis also consumes two molecules of nicotinamide adenine dinucleotide (oxidized; NAD+), an important electron acceptor in metabolism that must be regenerated for glycolysis to continue.1,2

In contrast to glycolysis, the reactions of the citric acid cycle occur within the mitochondria and only under aerobic conditions. In the presence of oxygen, pyruvate is shuttled into the mitochondria and converted to acetyl coenzyme A (acetyl CoA) by the pyruvate dehydrogenase (PDH) enzyme complex.1,2 Acetyl CoA enters the citric acid cycle and is completely oxidized to carbon dioxide, generating two intermediate molecules—nicotinamide adenine dinucleotide (reduced) and flavin adenine dinucleotide. Oxidative phosphorylation utilizes these intermediate molecules within the electron transport chain for the synthesis of ATP. Of the 36 to 38 net molecules of ATP generated during the metabolism of a single molecule of glucose under aerobic conditions, two are derived during glycolysis, two are generated in the citric acid cycle, and 32 to 34 are synthesized during oxidative phosphorylation (FIGURE 1).

Under anaerobic conditions, pyruvate is unable to enter the mitochondria and is preferentially transformed into lactate by the enzyme lactate dehydrogenase. The conversion of pyruvate to lactate regenerates the NAD+ required to continue glycolysis and anaerobic production of ATP.3,4 During anaerobiosis (tissue metabolism in the absence of oxygen), the cells rely entirely on glycolysis to meet their energy requirements. Because this process is much less efficient, the rate of glycolysis must increase to produce sufficient...
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**Box 1. Causes of Types A and B Hyperlactatemia**

<table>
<thead>
<tr>
<th>Type A</th>
<th>Type B</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Decreased Oxygen Delivery</strong></td>
<td><strong>Inadequate Oxygen Utilization</strong></td>
</tr>
<tr>
<td>• Hypotension</td>
<td>• Systemic inflammatory response syndrome</td>
</tr>
<tr>
<td>• Volume depletion</td>
<td>• Diabetes mellitus</td>
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<tr>
<td>• Blood loss</td>
<td>• Malignancy</td>
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<tr>
<td>• Cardiogenic shock</td>
<td>• Parenteral nutrition</td>
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<tr>
<td>• Septic shock</td>
<td>• Thiamine deficiency</td>
</tr>
<tr>
<td>• Severe anemia</td>
<td>• Congenital lactic acidosis</td>
</tr>
<tr>
<td>• Severe hypoxemia</td>
<td>• Mitochondrial dysfunction</td>
</tr>
<tr>
<td>• Carbon monoxide poisoning</td>
<td>• Drugs/toxins</td>
</tr>
<tr>
<td>• Inadequate oxygen delivery</td>
<td>• Ethylene/propane glycol</td>
</tr>
<tr>
<td><strong>Increased Oxygen Demand</strong></td>
<td>• Cyanide</td>
</tr>
<tr>
<td>• Exercise</td>
<td>• Bicarbonate</td>
</tr>
<tr>
<td>• Seizures</td>
<td>• Catecholamines</td>
</tr>
<tr>
<td>• Shivering</td>
<td>• Lactulose</td>
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</tbody>
</table>

*Sepsis and systemic inflammatory response syndrome often exhibit components of both types of hyperlactatemia.
*Congenital lactic acidosis is not thought to be important in veterinary medicine.
*This list includes only toxins or drugs to which horses may be exposed.

**Lactate Production in Disease**

Lactate has traditionally been considered to be a marker of tissue hypoxia and a dead-end product in carbohydrate metabolism. However, these concepts have been reevaluated in the past 3 decades. Decreased DO₂ and anaerobic metabolism are the most important causes of an increase in blood lactate concentration in humans and animals, and this is referred to as type A hyperlactatemia (BOX 1). In horses with sepsis, tissue hypoperfusion (due to hypovolemia), volume maldistribution, and, potentially, microvascular injury are common. Less commonly, in equine patients, a decrease in DO₂ may occur subsequent to impaired cardiac function, decreased oxygen-carrying capacity, or hypoxemia secondary to severe pulmonary disease. Hyperlactatemia that occurs under conditions in which DO₂ appears to be adequate is called type B hyperlactatemia (BOX 1), although in many cases, microvascular injury and focal hypoperfusion are difficult to exclude as causes of the increase in lactate concentration. Hyperlactatemia under aerobic conditions usually accompanies an intense systemic inflammatory reaction; some of the proposed mechanisms are discussed in the following sections.

**Box 2. Lactate as an Energy Source**

Lactate is an important carbohydrate intermediate in whole body energy metabolism. In vivo lactate turnover, at least in humans, is of a similar magnitude as glucose, alanine, or glutamine turnover, and the results of recent studies suggest that lactate is an alternative energy source for the brain during cerebral ischemia and for the heart during hemorrhagic shock.
conditions. Plasma catecholamine concentrations, particularly epinephrine, are increased during both hemorrhagic and septic shock and stimulate activity of the ubiquitous cell membrane Na+/K+-ATPase pump.\(^6,11\) Na+/K+-ATPase pumps have their own set of glycolytic enzymes that provide ATP and are not shared with those of the cellular energy metabolic apparatus. Pyruvate generated by the pump-associated glycolytic pathway is preferentially converted to lactate and then exported from the cell rather than fed into the citric acid cycle.\(^6,11\) To meet the increased ATP requirements of the activated Na+/K+-ATPase pumps, the rate of glycolysis is increased in response to increased concentrations of epinephrine and adenosine diphosphate, the latter being a by-product of Na+/K+-ATPase activity. In this scenario, stored muscle glycogen serves as the source of glucose (i.e., glucose-6-phosphate) and thus lactate.\(^6,11\)

### Inhibition of Pyruvate Dehydrogenase

PDH, the enzyme complex that links glycolysis to the citric acid cycle, is a key regulator of glucose metabolism.\(^12\) PDH activity is increased when the complex is dephosphorylated by PDH phosphatase and decreased when it is phosphorylated by pyruvate dehydrogenase kinase (PDK). Decreased activity of the PDH complex promotes the conversion of pyruvate to lactate rather than to acetyl CoA, and dysregulation of skeletal muscle PDH has been implicated in the development of hyperlactatemia during sepsis. Activity of the skeletal muscle PDH complex is decreased in experimentally induced sepsis\(^4\) and after infusion of lipopolysaccharide.\(^11\) The decrease in PDH activity is mediated by an increase in PDK activity and subsequent phosphorylation of PDH.\(^4,13\) Reportedly, the increase in PDK activity occurs secondary to increases in proinflammatory cytokines such as tumor necrosis factor–α (TNF-α) and interleukin-6 (IL-6).\(^13\) The role of PDH inhibition in hyperlactatemia is further supported by the ability of dichloroacetate, a chemical that inhibits PDK activity, to reduce lactate and exported from the cell rather than being fed into the citric acid cycle. Epinephrine concentrations are increased during shock, stimulating activity of the cell membrane Na+/K+-ATPase pump via increased cAMP concentrations. To meet the increased ATP requirements of the activated Na+/K+-ATPase pumps, the rate of glycolysis is increased in response to increased concentrations of epinephrine (via cAMP) and ADP. (ADP = adenosine diphosphate; ATP = adenosine 5′-triphosphate; cAMP = cyclic adenosine monophosphate).

### Lactate Production by Leukocytes

Approximately 80% of glucose metabolized by inflammatory leukocytes is converted to lactate. Haji-Michael et al\(^14\) suggest that lactate production in sepsis may be partially explained by the increase in glycolysis occurring in inflammatory cells sequestered within tissue beds. Using a cecal ligation and puncture model of sepsis in rats, this group reported that lactate production by peritoneal leukocytes was increased during sepsis compared with peritoneal leukocytes from sham-operated rats. Additionally, lactate production by leukocytes isolated from human intensive care patients was much higher than that by leukocytes obtained from healthy people when stimulated in vitro with lipopolysaccharide.\(^11\) On a wet-weight basis, leukocytes can produce considerably more lactate than tissues traditionally considered to be "lactate producers" (i.e., skeletal muscle, intestine); however, the relevance of these in vitro observations is unclear.

### Impaired Hepatic Clearance

Patients with liver failure may be unable to metabolize lactate effectively, which can result in an increase in the blood lactate concentration.\(^1\) Using a canine model, Chrusch et al\(^7\) showed that impaired hepatic clearance may contribute to hyperlactatemia during sepsis. Hepatic function may be reduced in sepsis as a result of hepatocellular dysfunction or decreased hepatic perfusion subsequent to hypovolemia or volume maldistribution. In a study of septic but hemodynamically stable human patients, Levraut et al\(^15\) reported that blood lactate concentrations returned to baseline more slowly after infusion of exogenous lactate in patients with hyperlactatemia (≥2 mmol/L) compared with patients with normal blood lactate concentrations (≤1.5 mmol/L). These findings support the contention that hepatic metabolism of lactate is decreased during sepsis and plays a role in the development of hyperlactatemia. However, the results of other studies have cast some doubt on the role of impaired hepatic metabolism as a cause of hyperlactatemia. For example, in a rodent model of sepsis, Severin et al\(^16\) showed that hepatic extraction of lactate was increased during lipopolysaccharide infusion and suggested that impaired clearance of lactate by tissues other than the liver may be important in hyperlactatemia. More recently, Revelly et al\(^17\) examined lactate clearance in patients with septic or cardiogenic shock and found...
that it was similar to that in healthy volunteers. These findings agree with the earlier report\textsuperscript{24} that the hepatopancreatic region cleared, rather than produced, lactate in patients with multisystem organ failure but without obvious hepatic involvement. Thus, the liver’s role in hyperlactatemia during sepsis is unclear; however, it seems likely that impaired hepatic clearance contributes to increases in blood lactate concentration in some patients with severe liver failure.

**Other Causes of Hyperlactatemia**

Hyperlactatemia may develop for several other reasons, including impaired mitochondrial function\textsuperscript{9} and hypermetabolism with increased tissue glycolysis.\textsuperscript{20} Occasionally, an increase in blood lactate concentration occurs after aggressive fluid resuscitation of extremely hypovolemic patients.\textsuperscript{21} This is presumably due to tissue washout of lactate as tissue perfusion is reestablished. Propylene glycol toxicosis and administration of exogenous catecholamines (i.e., epinephrine and norepinephrine) also increase the blood lactate concentration, as does administration of sodium bicarbonate under some circumstances.\textsuperscript{1,22} Hyperlactatemia has also been associated with certain hematologic malignancies in people\textsuperscript{23} and has recently been reported in a 2-year-old angus heifer with lymphosarcoma.\textsuperscript{24} Some neoplastic cells apparently have very high rates of glycolysis and are thought to be a source of lactate. The coexistence of hyperlactatemia and hematologic neoplasia is associated with an extremely poor prognosis in affected humans.\textsuperscript{25}

**The Source of Lactate in Health and Disease**

Under normal physiologic conditions, the tissues producing the largest amounts of lactate are the skin, erythrocytes, and skeletal muscles.\textsuperscript{1} Erythrocytes lack mitochondria and the enzymes needed to metabolize pyruvate and are, therefore, obligate lactate producers.\textsuperscript{25} Other cells intermittently operate under anaerobic conditions and consequently produce lactate.\textsuperscript{26} As a result, the average human produces approximately 0.8 mmol/kg/h of lactate, which is rapidly metabolized, primarily by the liver and, to a lesser extent, the kidneys and skeletal muscles.\textsuperscript{1} During sepsis, skeletal muscle is thought to be the primary source of lactate because of its large mass.\textsuperscript{4,5} However, several investigators have suggested that the lungs\textsuperscript{4,27,28} or splanchic (gastrointestinal [GI] and/or hepatic) tissues may become significant lactate producers during severe disease in some patients.\textsuperscript{7}

Normal lungs neither produce nor consume lactate in subjects at rest or during mild exercise; however, injured pulmonary tissue may produce lactate.\textsuperscript{29} Pulmonary production of lactate is directly related to the severity of lung disease, with generalized, severe injury required for net lactate production.\textsuperscript{27,28} Interestingly, bacterial infection does not seem to be required, as pulmonary production of lactate in patients with acute lung injury and concurrent bacterial pneumonia was not significantly different from pulmonary production in patients with acute lung injury alone.\textsuperscript{29} Although pulmonary production of lactate may be increased in patients with severe lung disease, arterial lactate concentrations have not correlated with the magnitude of pulmonary lactate production in some studies, suggesting that the lungs are not the primary source of hyperlactatemia in these patients.\textsuperscript{28}

The difference between arterial and venous lactate concentrations across the GI tract are extremely small or even slightly negative, indicating that GI tissues do not normally produce lactate and may actually consume it.\textsuperscript{7,29} Although these tissues produce lactate during ischemia, the situation is far less clear in sepsis. In most experimental models of sepsis, lactate fluxes across the GI tract remain close to zero,\textsuperscript{26} although selected experimental studies have reported increases in lactate production by the GI tract under these conditions.\textsuperscript{7} One study reported that the hepatopancreatic region was an uncommon source of hyperlactatemia in humans with severe sepsis; however, lactate production by the GI tract and clearance by the liver could not be separated.\textsuperscript{20}

**L- and D-Isomers of Lactate and Normal Concentrations**

Lactate exists as L- and D-isomers. Mammalian cells almost exclusively produce L-isomer lactate, while bacteria produce D-isomer lactate.\textsuperscript{31} In most healthy mammals, L-isomers exist in millimolar concentrations, whereas D-isomers normally exist only in nanomolar concentrations. Hyper-D-lactatemia occurs only rarely in humans and is primarily observed in patients with short bowel syndrome.\textsuperscript{31} In contrast, increases in D-lactate concentration are not uncommon in ruminants with excessive GI carbohydrate fermentation and subsequent lactobacilli overgrowth with D-lactate production.\textsuperscript{21}

Normal L-lactate concentrations in healthy, unstressed humans are 0.5 to 1.0 mmol/L. In critically ill humans, normal L-lactate concentrations are <2 mmol/L; concentrations >2 mmol/L indicate hyperlactatemia.\textsuperscript{1} The term *lactic acidosis* is used for a persistently increased blood lactate concentration (usually >5 mmol/L) associated with a metabolic acidosis.\textsuperscript{1} Similar definitions have not been developed for horses; however, many clinicians consider 1.5 mmol/L to be the upper end of normal blood lactate concentrations in adult horses,\textsuperscript{32} and most healthy adult horses have a blood lactate concentration of <1 mmol/L. Healthy neonatal foals tend to have high blood lactate concentrations at birth that decrease within a few days; for example, blood lactate concentrations in 14 healthy foals decreased from 2.38 ± 1.03 mmol/L at birth to 1.24 ± 0.33 at 24 hours and 1.08 ± 0.27 at 48 hours.\textsuperscript{32} Blood lactate concentrations in healthy foals older than 1 week are similar to those in adult horses. The reason for the increase in blood lactate concentrations in healthy newborn foals is unclear, but it may be related to immature hepatic function or the use of lactate as an energy substrate early in life.\textsuperscript{32} A similar phenomenon occurs in other species: blood lactate concentrations of 2.6 ± 0.7 mmol/L have been documented in healthy 48-hour-old term human neonates,\textsuperscript{33} and venous lactate concentrations are significantly higher in healthy puppies for the first 28 days of life than concentrations in adult dogs.\textsuperscript{34}

**Measuring the Lactate Concentration**

Although lactate may be measured in plasma or whole blood, most lactate analyzers used in clinical practice measure plasma lactate concentration. Depending on the species, there can be a
large difference between plasma and whole blood concentrations of lactate. For example, the plasma lactate concentration is approximately half that of whole blood in healthy adult horses at rest, while the intraerythrocyte lactate concentration is similar to that of whole blood.\textsuperscript{35} In contrast, plasma and whole blood lactate concentrations are similar in humans, but the intraerythrocyte concentration is much lower than that of whole blood.\textsuperscript{36} The physiologic state of the animal is also important; in exercising horses, plasma and intraerythrocyte lactate concentrations increase, but at different rates, so the plasma lactate concentration exceeds the intraerythrocyte concentration.\textsuperscript{35}

Although lactate analyzers are commonly used in large referral hospitals, the ability to measure lactate concentration has only recently become readily accessible to ambulatory practitioners. Fortunately, inexpensive, pocket-sized, point-of-care lactate analyzers designed for use by human athletes are now available. The accuracy and reliability of several of these portable lactate analyzers have been established using blood samples from a number of species, including healthy exercising horses\textsuperscript{37} and horses evaluated as emergency admissions to a referral hospital.\textsuperscript{38} Because point-of-care analyzers decrease analytic time and patient costs, these devices are being used in human and veterinary critical care facilities, where rapid turnaround of test results is imperative.

In one study, a point-of-care monitor (Accutrend, Roche Diagnostics) was assessed in adult horses admitted to a referral hospital as emergency cases.\textsuperscript{38} This monitor uses test strips similar to those used in handheld dextrometers and has a test area composed of four layers. In normal usage, a drop of whole blood is applied to the test area and moves through a protective mesh; erythrocytes are trapped within the second layer, allowing plasma to diffuse into the third layer, where a colorometric reaction catalyzed by lactate oxidase occurs. The degree of color change is measured using reflectance photometry and depends on the concentration of lactate in plasma. In heparinized plasma samples, lactate concentrations determined using this point-of-care monitor correlated extremely well with values obtained using a standard laboratory-based method. However, the point-of-care monitor was less accurate when whole blood samples were used, particularly when the hematocrit exceeded 40%.\textsuperscript{37,38} The reasons for decreased accuracy when using whole blood samples are unknown but may be related to the way in which equine erythrocytes pack in the test strips, as this may trap plasma or interfere with the photometric light source. Although values obtained with whole blood are less accurate than those obtained using plasma, the former may be sufficient to identify trends in lactate concentration when centrifugation is not possible.\textsuperscript{38} Alternatively, samples may be collected into tubes containing sodium fluoride (see below) and (ideally) stored on ice until they can be centrifuged and the plasma analyzed. Because the point-of-care analyzer uses only 25 μL of blood, centrifugation of one or two microhematocrit tubes will provide adequate plasma if a larger centrifuge is not available. If a centrifuge is not readily available, collecting whole blood into a sodium fluoride tube and allowing it to settle is often sufficient to obtain a useful sample.

The site of blood collection (arterial versus venous, and choice of vein) has some effect on the measured lactate concentration, but these differences typically are clinically insignificant.\textsuperscript{39} Unless the clinician wants to assess pulmonary function, venous blood samples are usually adequate for lactate measurement and are easier to obtain than arterial samples. A slight increase in the lactate concentration may occur with prolonged occlusion of a vein when a blood sample is drawn, and blood lactate concentrations may increase in struggling animals.\textsuperscript{32} Lactate-containing fluid solutions that are inadequately cleared from intravenous catheters may falsely increase the measured lactate concentration in samples collected from these catheters.\textsuperscript{22} Similarly, fluids that lack lactate may dilute the blood, resulting in falsely low lactate concentrations if the fluid is not completely removed from the intravenous catheter before the sample is collected.\textsuperscript{22}

Erythrocytes continue to produce lactate ex vivo. Therefore, it is essential for samples to be analyzed within 5 to 10 minutes of collection because the lactate concentration may increase considerably with storage; this is particularly true for blood samples collected into tubes containing lithium heparin and stored at room temperature.\textsuperscript{40} If not analyzed immediately, blood should be collected into tubes containing sodium fluoride–potassium oxalate and chilled (0°C to 4°C [32°F to 39.2°F]). The combination of sodium fluoride–potassium oxalate inhibits several glycolytic enzymes, preventing further lactate production; however, the use of sodium fluoride may alter other variables, including the hematocrit and the glucose concentration.\textsuperscript{40}

The methodologies used to measure lactate in laboratory-based and portable analyzers are isomer specific, measuring only L-lactate. Special assays are required to determine D-lactate concentrations,\textsuperscript{31} although the presence of D-lactic acidosis may be suggested by an increased anion gap in a patient with a normal L-lactate concentration or an L-lactate concentration that does not account for most of the anion gap.\textsuperscript{31}

**Conclusion**

Inadequate DO\textsubscript{2} and tissue hypoxia remain the most important causes of increased blood lactate concentrations; however, it is important to recognize that hyperlactatemia may occur in the presence of normal tissue oxygenation. Under the latter conditions, hyperlactatemia often indicates a severe inflammatory response or, less commonly, reflects impaired hepatic function. In patients with increased blood lactate concentrations, initial clinical efforts should be directed toward ensuring adequate arterial oxygenation and tissue perfusion. Several readily available, inexpensive, point-of-care analyzers allow rapid, accurate lactate measurement by equine practitioners. However, it is important to recognize the limitations of these analyzers, especially regarding sample type, to ensure appropriate interpretation of results.

**References**

1. Which statement regarding glycolysis is incorrect?
   a. It only occurs in the presence of oxygen.
   b. It generates two molecules of ATP and hydrogen ions for every molecule of glucose metabolized.
   c. It occurs within cytoplasm.
   d. It requires regeneration of NAD+ to proceed.

2. The conversion of pyruvate to lactate
   a. is catalyzed by the PDH enzyme complex.
   b. regenerates NADH, allowing glycolysis to continue.
   c. consumes hydrogen ions and is, therefore, alkalinizing rather than acidifying.
   d. occurs in the mitochondria.

3. Which of the following is a cause of type B hyperlactatemia?
   a. neonatal isoeerythrolysis
   b. severe pleurpneumonia
   c. hypoxic-ischemic encephalopathy of neonates with prolonged seizure activity
   d. cyanide toxicosis

4. Which statement is incorrect regarding the association between Na+/K+-ATPase activity and hyperlactatemia in sepsis?
   a. Catecholamine concentrations are increased during septic shock.
   b. The increase in catecholamine concentrations stimulates cell membrane Na+/K+-ATPase pump activity.
   c. Pyruvate produced by glycolytic enzymes associated with Na+/K+-ATPase is preferentially fed into the citric acid cycle.
   d. The increase in catecholamine concentrations stimulates glycolysis to generate ATP to support Na+/K+-ATPase pump activity.

5. Activity of the PDH complex is increased by
   a. dephosphorylation by PDK.
   b. phosphorylation by PDH phosphatase.
   c. dichloroacetate—a chemical that inhibits PDK activity.
   d. dichloroacetate—a drug that increases PDH phosphatase activity.

6. The arteriovenous difference in lactate concentration across normal lungs and the GI tract is usually close to zero. However, during disease, these tissues may become lactate producers. Which of the following is correct?
   a. Lactate production by pulmonary tissue is inversely correlated with the severity of lung injury.
   b. The lungs only become lactate producers in the presence of bacterial infection.
   c. Most studies show that the GI tissues become net lactate producers during sepsis.
   d. The GI tissues become lactate producers during ischemia.

7. Which of the following statements is correct?
   a. In the blood of healthy animals, α-lactate has a similar concentration to that of β-lactate but cannot be measured by most analyzers.
   b. Hyper-α-lactatemia has been frequently documented in neonatal foals with GI disease and sepsis.
   c. Healthy foals commonly have higher blood lactate concentrations at birth than adults, but concentrations decrease to adult levels within hours of birth.
   d. A blood lactate concentration of 1.5 mmol/L is often considered the upper end of normal for adult horses; however, many horses have concentrations of <1 mmol/L.

8. If the lactate concentration cannot be analyzed shortly after blood collection, blood samples should be stored in tubes containing
   a. sodium heparin.
   b. lithium heparin.
   c. sodium fluoride–potassium oxalate.
   d. serum separator gel.

9. Which of the following is not expected to artifactually increase the measured blood lactate concentration?
   a. prolonged occlusion of the vein during sample collection
   b. incomplete flushing of the catheter from which the sample was collected after lactate-containing fluids were administered
   c. incomplete flushing of the catheter from which the sample was collected after fluids that do not contain lactate were administered
   d. allowing the sample to sit at room temperature for a prolonged period before analysis

10. Which statement best describes the performance of a commercial point-of-care lactate monitor that was assessed for use in adult horses under emergency conditions?
    a. Agreement between the point-of-care monitor and a laboratory-based method of lactate measurement was excellent for heparinized plasma samples.
    b. Agreement between the point-of-care monitor and a laboratory-based method of lactate measurement was excellent for whole blood samples.
    c. Accuracy improved when whole blood samples with packed cell volumes >40% were used for analysis.
    d. Accuracy was poor in emergency cases because these monitors are unable to distinguish α-lactate from β-lactate.